"DEVELOPMENT AND VALIDATION OF ANALYTICAL METHODS FOR SELECTED PHARMACEUTICAL DRUGS AND COMBINATIONS BY QUALITY BY DESIGN AND GREEN CHEMISTRY APPROACH"

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1. Abstract of proposed work plan/ problem:

The increasing emphasis on sustainable practices in pharmaceutical analysis has driven the need for environmentally friendly analytical methods. Traditional techniques often rely on hazardous chemicals and solvents, posing significant environmental risks. This research aims to develop and validate novel analytical approaches that minimize environmental impact while maintaining high sensitivity, specificity, and accuracy. By leveraging advancements in technologies such as high-performance liquid chromatography (HPLC) and Ultra Performance Liquid Chromatography (UPLC), High Performance Thin Layer Chromatography (HPTLC), Ultra Violet Spectroscopy (UV) etc. This study seeks to create efficient, cost-effective, and less polluting methods. Compliance with regulatory standards set by bodies like the FDA and ICH is a key focus, ensuring that the developed methods are both effective and environmentally benign. The adoption of greener analytical techniques not only reduces operational costs and waste disposal expenses but also offers direct benefits to public health by minimizing the release of harmful substances. This research will explore innovative materials, techniques, and approaches, contributing to scientific innovation and the advancement of sustainable pharmaceutical analysis.

Keywords: Green analysis, QbD, Method Development, analysis, validation.

2. Introduction:

In the pharmaceutical industry, the analysis of pharmaceuticals is a critical process that ensures the safety, efficacy, and quality of medications before they are made available to consumers. This precise analysis includes several techniques used to understand the physical and chemical properties of pharmaceutical substances. Key aspects include chemical analysis whereby the active ingredients and excipients in a drug are identified, and quantified using such techniques as High-Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC). Physical analysis examines aspects such as particle size and shape through techniques like microscopy and X-ray diffraction. In stability testing, drugs are assured to remain effective over their shelf lives by subjecting them to various environmental conditions. Biopharmaceutical analysis determines the drug's absorption, distribution, metabolism, and excretion in the body. It ensures that the products are free from harmful microorganisms through microbiological testing. In this way, pharmaceutical companies can meet regulatory standards and ensure safe and effective treatments for patients. (Eldin et al., 2016)

Current Analytical Practices:

Reagents and Solvents: The traditional practice often employs toxic chemicals and hazardous organic solvents like methanol and acetonitrile with adverse effects on human beings and the environment.

Energy Intensity: Techniques such as High-Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC) require large inputs of energy for running and evaporation of solvents, leading to a more extensive carbon footprint.

Waste Production: The use of significant volumes of solvents and reagents leads to considerable chemical waste that is difficult to manage and dispose of.

Performance-Based Approach: In the process of ensuring analytical performance, the conventional techniques tend to overlook the environmental impact and sustainability of the analytical process. (Saroj et al., 2018)

Green Analytical Techniques by QbD:

Safer Reagents and Solvents: Green methods stress the use of safer, more sustainable reagents and solvents, like water or ethanol, which are less toxic and environment-friendly. Solvent-free techniques are also pursued to minimize chemical hazards.

Energy Efficiency: The green approach involves adopting energy-efficient instruments and processes. Miniaturization of analytical systems and using ambient conditions reduce energy consumption.

Waste Minimization: Through the optimization of analytical procedures to reduce reagent and solvent quantities, green analytical methods significantly reduce chemical waste. Techniques such as microextraction and solid-phase extraction are utilized to achieve this goal.

Integration of QbD Principles: The integration of QbD principles will allow the systematic development of robust, green methods. Through DoE, critical method parameters can be identified, and the establishment of a design space is ensured to provide consistency of performance while maintaining principles from green chemistry.

Holistic Approach: Green methods will have high analytical performance but also be considering the overall sustainability of the process, for example, life cycle analysis for the development and implementation of the method and disposal of waste.

Integration of green analytical chemistry with QbD would bring about a holistic approach in the development of sustainable and effective analytical methods. Such practices adopted by the pharmaceutical industry can satisfy regulatory standards, ensure the safety of the product, and minimize the ecological footprint of pharmaceutical analysis. (Saroj et al., 2018)

Analytical method development and validation are crucial steps in ensuring the accuracy and reliability of analytical data in pharmaceuticals. Analytical method development involves creating a procedure to accurately measure a specific compound or set of compounds within a sample. This process includes selecting appropriate techniques, such as chromatography or spectroscopy, and optimizing conditions like mobile phase composition and detection parameters. Once a method is developed, it must undergo

validation to ensure it produces consistent and reliable results. Validation involves testing the method for several parameters, including accuracy, precision, specificity, sensitivity, linearity, and robustness. By rigorously developing and validating analytical methods, pharmaceutical companies can ensure their products meet regulatory standards and provide safe, effective treatments for patients.(Dhoru et al., 2020)

In recent years, the pharmaceutical industry has increasingly prioritized sustainable practices, recognizing the environmental impact of traditional analytical methods. Conventional techniques often involve the use of hazardous chemicals and solvents, which pose significant risks to the environment. This has led to a growing demand for the development of environmentally friendly analytical methods that do not compromise on sensitivity, specificity, or accuracy. (Mehta et al., 2024, Nakov et al., 2023)

Green analytical chemistry (GAC) is an emerging field that focuses on developing and implementing analytical methods that minimize environmental impact and reduce hazardous waste. It aims to replace traditional, often toxic, solvents and reagents with safer, more sustainable alternatives.[4] By incorporating principles such as atom economy, energy efficiency, and the use of renewable resources, GAC seeks to make analytical processes more eco-friendly. This approach not only benefits the environment but also enhances safety for laboratory personnel and reduces costs associated with waste disposal.(Al-Shatti et al., 2023)

QbD approaches for green analytical methods combine the principles of green chemistry with the systematic framework of QbD to provide an environmentally friendly analytical procedure. In essence, this involves optimization of analytical methods to use as few hazardous reagents as possible, minimize waste production, and maximize energy efficiency. Key elements include DoE for the identification of the most critical method parameters as well as a design space that ensures robust and environmentally friendly performance. By focusing on critical quality attributes (CQAs) and critical process parameters (CPPs), QbD approaches ensure that analytical methods are not only effective but also sustainable (Bairagi et al., 2024).

This research focuses on creating and validating novel analytical approaches that minimize environmental impact. By leveraging advancements in high-performance liquid chromatography (HPLC) and other analytical procedures, the study aims to develop

methods that are not only efficient and cost-effective but also less polluting. A key aspect of this research is ensuring compliance with regulatory standards set by bodies such as the FDA and ICH, guaranteeing that the methods developed are both effective and environmentally benign.

The adoption of greener analytical techniques offers numerous benefits, including reduced operational costs and lower waste disposal expenses. Additionally, these methods contribute to public health by minimizing the release of harmful substances into the environment. This research will explore innovative materials, techniques, and approaches, contributing to scientific innovation and the advancement of sustainable pharmaceutical analysis. By focusing on these goals, the study aims to pave the way for more sustainable practices in the pharmaceutical industry. (Nakov et al., 2023)

As a move toward sustainable and environmentally friendly practices, it is important for the pharmaceutical industry to embrace green analytical chemistry (GAC) and Quality by Design (QbD) principles. Traditional methods of analysis, although delivering reliable and accurate results, tend to employ hazardous solvents and reagents, consume huge amounts of energy, and generate significant chemical waste. The proper practice further poses health risks to lab personnel and environmental hazards owing to improper disposal. Having strong interest in sustainable methodologies to produce research, I suggest designing, developing, and validating a green analytical method using Quality by Design approaches to confront these challenges. (Al-Shatti et al., 2023)

Current Analytical Approach	**Green Analytical Methods with QbD Approach**
Environmental Impact	
Use highly hazardous chemicals and solvents, causing significant damage to the environment and human health.	Utilize environmentally friendly solvents and techniques, reducing the environmental footprint.
Need for New Methods	
High analytical techniques can be harmful and inefficient.	New methods aim to maintain sensitivity and specificity while being eco-friendly, using the QbD approach to minimize trials and errors.

Technological Advancement	
Relies on conventional techniques that may not be cost-effective or efficient.	Employs advanced technologies like high-performance liquid chromatography (HPLC) for more efficient and less polluting methods, guided by QbD principles.
Regulatory Compliance	
Must meet stringent regulatory standards but often lacks focus on environmental sustainability.	Designed to comply with regulatory standards (e.g., FDA, ICH) while prioritizing environmental sustainability, ensuring robust and reliable methods through QbD.
Benefits	
Can be costly and generate significant waste, posing risks to public health.	Reduces operational costs, lowers waste disposal expenses, and contributes to public health by minimizing harmful emissions, with enhanced method development efficiency through QbD.
Research Goals	
Focuses on traditional practices without significant innovation in sustainability.	Aims to explore novel analytical methods, promote scientific innovation, and develop green pharmaceutical analysis, leveraging QbD to optimize method development.
Summary	
Traditional methods often overlook environmental issues, leading to sustainability challenges.	Green methods with QbD address environmental concerns, promote sustainability, public health, and regulatory compliance, and open doors for more sustainable practices in the pharmaceutical sector.

3. Review of Literature & Development in the Subject:

The development and validation of green analytical methods have gained significant attention in recent years due to the increasing emphasis on environmental sustainability and regulatory requirements. This review highlights various approaches and methodologies employed in the development of eco-friendly analytical protocols.

1. **Hashmi and Alegete (2024):** A QbD-assisted green UHPLC method was developed for the quantification of Tolvaptan, characterized by its simplicity, rapid execution, cost-effectiveness, and stability. The method employed an ACE Excel super C18 column with a mobile phase consisting of acetonitrile and water in a 95:5 ratio, achieving an accuracy exceeding 99% and a correlation coefficient above 0.999. Additionally, the method demonstrated stability-indicating capabilities during forced degradation testing, and its environmental sustainability was confirmed through assessments using Complex GAPI and the Analytical Eco scale, highlighting its eco-friendliness. The method was validated in accordance with ICH guidelines, ensuring its reliability and robustness for practical applications. (Hashmi & Alegete, 2024)

2. **Kamal et al. (2023):** A green and rapid HPLC method was developed for the simultaneous analysis of fluorescein sodium and benoxinate hydrochloride, achieving results in just four minutes. The optimization process utilized fractional factorial and Box–Behnken designs, with the method demonstrating high recovery rates of 99.21% for benoxinate and 99.88% for fluorescein. The greenness of the method was evaluated using analytical eco-scale and HPLC-EAT tools, resulting in scores of 90 and 4.21, respectively, and it was successfully applied to stress degradation studies and formulated eye drops without any interference. (Kamal et al., 2023)

3. **Yabré et al., (2020):** The research work of Yabré et al. (2020) discusses the development of a sustainable reversed-phase high-performance liquid chromatography (RP-HPLC) method for the impurity profiling of two prominent pharmaceutical compounds, namely artesunate and amodiaquine. The authors implemented Quality by Design (QbD) approaches in developing a robust analytical protocol that utilizes ethanol as a green solvent, thus greatly reducing the

environmental impact associated with traditional organic solvents. The method was validated based on ICH Q2 (R1) guidelines, resulting in satisfactory resolution in separating impurities, and it has applicability both to raw material and fixed-dose formulation that would make for a viable approach in pharmaceutical quality control in resource-limited labs. (Yabré et al., 2020).

4. **Fares et al., (2022):** This study developed an eco-friendly high-performance liquid chromatography technique for the simultaneous analysis of deferasirox (DFX) and deferiprone (DFP) in biological fluids by employing an analytical quality-by-design approach to optimize method parameters. Ethanol combined with acidic water at pH 3.0 was used as a mobile phase, and optimum separation was achieved. The method was validated according to FDA guidelines, with excellent sensitivity and accuracy. Moreover, pharmacokinetic investigations demonstrated enhanced bioavailability following the co-administration of DFX and DFP, indicating a possibility for synergistic therapeutic approaches in the management of thalassemia. (Fares et al., 2022)

5. **Venkateshwarlu et al. (2024):** The study was designed to come up with a green analytical method for the estimation of Favipiravir using a QbD-based HPLC approach. Optimized conditions included a mobile phase of 70% ethanol, a flow rate of 1.0 ml/min, and a run time of 10 minutes. The method was validated according to ICH guidelines, showing accuracy, precision, and robustness. The method was also assessed in terms of its greenness by employing NEMI, GAPI, and AGREE metrics, which scored 0.82, thereby being an eco-friendly process. Conclusion The method is efficient, safe, and suitable for routine quality control of Favipiravir in pharmaceutical formulations. (Venkateshwarlu et al., 2024)

6. **Perumal et al. (2022):** This paper presents a novel and green-friendly high-performance liquid chromatography (HPLC) method, designed for simultaneous separation and quantification of the anxiolytic drugs escitalopram (ESC) and etizolam (ETZ). The present work highlights the importance of the principles of green chemistry in pharmaceutical analysis by improving the sustainability of analytical procedures. Elaboration on the development of this technique through Quality by Design (QbD) methodology is necessary because this is a very crucial approach to reducing environmental consequences related to pharmaceutical

analysis with maintaining precision and dependability of acquired results. The outcome necessitates more sustainable solvents and methodologies in the scientific world for environmentally conscious practice within the pharmaceutical sector. (Perumal et al., 2022)

7. **Jatte et al. (2021):** This article analyzes and validates Lisinopril and Hydrochlorothiazide using Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) with the approach of Quality by Design. It discusses and prepares the standard solution conditions and adjusts the chromatographic with a gradient system UV detector along with enhancing drug separation along with time by minimizing this analysis through Taguchi Screening and Multiple Linear Regression at Box Behnken design. Method validation indicates the accuracy, precision, and reliability of the developed tablet dosage methods. It includes forced degradation studies for drug stability assessment. Results show that the methods are suitable for routine quality control with satisfactory recovery rates and low standard deviations. The study brings out the necessity for optimizing and validating methods in pharmaceutical analysis to accurately check drug formulations.(Jatte et al., 2021)

8. **Chavan and Gandhimathi (2023):** In the paper the quality by design methodology is seen as one that enhances pharmaceutical analysis to ensure the quality of drugs. It focuses on how the new analytical techniques help develop reliable and cost-effective methods in the fast-growing pharmaceutical industry through QbD in the product's lifecycle. Authors Expository Discuss the role of method operable design regions and risk assessment in improving analytical methods in response to the requirements of regulations towards enhanced overall quality and safety of pharmaceutical products.(Chavan & Gandhimathi, 2023)

9. **Ahmad et al. (2022):** The study conducted by Ahmad et al. (2022) aimed to develop a stability-indicating RP-HPLC method for Naproxen and Pantoprazole using a Quality by Design (QbD) approach. The method was validated for various parameters, including linearity, precision, accuracy, limit of detection (LOD), and limit of quantitation (LOQ). The method was found to be linear for Naproxen at 10-50 µg/ml and Pantoprazole at 4-20 µg/ml without interfering peaks; thus, it was concluded that a strong, sensitive, and accurate method had been established in

accordance with the regulatory requirements for pharmaceutical analysis.(Ahmad et al., 2022)

10. **Sharma et al. (2020):** Critical parameters were identified by evaluation of the current analytical method through risk assessment and factor screening. The optimization of the critical parameters used a 3-factor-3-level-17-run Box Behnken Design. The optimal performance of the method was obtained through numerical and graphical optimization. This includes a C8 column with an 80:20 v/v acetonitrile-water mobile phase at a flow rate of 0.5 mL/min with an injection volume of 5 µL at a wavelength of 267 nm. The method validated as a good efficacy and sensitivity toward determination of chrysin content in work and plasma standards. LOD came at a high sensitivity at 0.028 µg/mL and LOQ was determined to lie at 0.075 µg/mL. From the accuracy experiments, 98.34% through 104.80%, high accuracy results came, and recovery occurred between such values. This method is useful both qualitatively and quantitatively in analyzing chrysin. A score of 81 for eco scale penalty points shows that it's a greener analytical method. (Sharma et al., 2020)

11. **Arunagiri et al. (2024):** The research focused on developing eco-friendly UV spectrophotometric methods for analyzing Aceclofenac (ACE), Paracetamol (PAR), and Tramadol (TRM). Utilizing techniques such as the Double Divisor Ratio Spectra Method (DDRSM) and Area Under the Curve (AUC), the study achieved accurate drug quantification with linear calibration curves, validated according to ICH guidelines. The methods demonstrated a high level of eco-friendliness, scoring favorably on green metrics such as GAPI, AGREE, and AES, indicating their reliability, cost-effectiveness, and suitability for routine pharmaceutical analysis.(Arunagiri et al., 2024)

12. **Robert (2023):** The article Green Analytical Chemistry (GAC) by Marco Robert of the University of Bologna, Italy, supports the use of eco-friendly approaches in the field of chemical analysis. The concept stresses the use of safer reagents and solvents, with less hazardous waste production and consumption of energy, as well as using in situ analytical techniques. GAC benefits include environmental protection, reduced pollution, cost effectiveness in the long run, and regulatory compliance. Its scope of applications ranges from pharmaceutical development,

ecological surveillance, food security, sustainable energy innovations, and waste disposal strategies, yet challenges remain in the need for further research and standard methodologies.(Robert, 2023)

13. **Yenduri et al. (2024):** The study evaluates the environmental impact of UV-spectroscopy techniques for analyzing combinations of anti-hypertensive drugs, specifically Amlodipine besylate and Telmisartan. Key tools used include the National Environmental Method Index (NEMI), Raynie and Driver Tool, Analytical Eco-Scale, and AGREE (Analytical GREEnness). All methods received an Analytical Eco-scale score of 85, indicating a generally good level of environmental friendliness. Methods 4 and 6 were highlighted as greener choices, earning an AGREE score of 0.67. Methods 2 and 7 scored lower, with most using methanol or HCl as solvents. Methods 4 and 6 were identified as the most environmentally friendly, while Method 7 was the least green. The study emphasizes the importance of developing eco-friendly methods that adhere to GAC principles and suggests integrating White Analytical Chemistry (WAC) principles in future method development.(Yenduri et al., 2024)

14. **Babar et al. (2022):** The developed HPLC method demonstrated high sensitivity and robustness, with validation studies confirming its reliability across various conditions. The method showed excellent linearity, high recovery rates, and precision for both intra-day and inter-day precision. The method's robustness was assessed through various parameters, confirming its capability to withstand minor variations without significant impact on performance.The study successfully demonstrated the application of QbD principles in developing a HPLC method for Tamoxifen, demonstrating its simplicity, rapidity, sensitivity, and cost-effectiveness. The findings highlight the critical role of risk assessment and optimization in achieving reliable analytical results, ultimately contributing to improved pharmaceutical quality.

From the comprehensive literature review conducted as listed above, it is observed that there is a significant gap in research focused on designing analytical methods for pharmaceuticals that are ecologically sustainable. This deficiency has given impetus to the proposed research aims to develop innovative analytical methods with significantly fewer trials using the Quality by Design (QbD) approach. This research will also incorporate the

use of environmentally acceptable solvents with lower toxicity. Once developed, these methods will be thoroughly assessed for their greenness using various available tools and software packages. Developed methods were validated as per the regulatory guidelines.

4. Objectives of the Proposed Research Work:

Aim

The primary aim of this research is to, "Development and Validation of Analytical Methods for Selected Pharmaceutical Drugs and Combinations by Quality by Design and Green Chemistry Approach"

Objectives

This proposed research aims to develop and validate sustainable analytical methods by focusing on the following objectives:

- **To review and identify current analytical methods:** Conduct a comprehensive literature review to identify existing analytical techniques and their applications in pharmaceutical analysis.
- **To apply Quality by Design (QbD) principles:** Implement QbD approaches to ensure robustness, reliability, and reproducibility of the developed analytical methods.
- **To develop novel green analytical methods:** Innovate and optimize new analytical methods that minimize the use of hazardous chemicals and reduce environmental impact.
- **To validate the developed methods:** Perform method validation according to ICH guidelines, ensuring accuracy, precision, specificity, linearity, and robustness.
- **To assess the Greenes of Developed Method:** Evaluate the environmental benefits of the developed methods compared to traditional analytical techniques, focusing on waste reduction, energy consumption, and overall sustainability this can be done by available softwares like AGREE, GAPI etc. Apply the developed methods to real-world pharmaceutical samples to demonstrate their effectiveness and practicality in routine quality control and regulatory compliance.

5. Methodology to be adopted:

The following methodology are adopted for the research work completion

Selection of Pharmaceutical Drugs and Combinations:

- Identify and select the pharmaceutical drugs and combinations to be analyzed from the literature review.

Procurement of drugs and chemicals:

- Procure the selected pharmaceutical drugs, combinations, required solvents and other chemicals from reliable sources.

Development of Analytical Method:

- Utilize the Quality by Design (QbD) approach to develop the analytical method.
- Select suitable solvents that are environmentally friendly.

Validation of Method:

- Validate the developed method according to ICH guidelines.
- Ensure accuracy, precision, linearity, limit of detection (LOD), limit of quantification (LOQ), and robustness etc.

Assessment of Method for Greenness:

- Evaluate the environmental benefits of the developed methods compared to traditional analytical techniques.
- Use available software tools like AGREE, NEMI and GAPI etc. for the assessment.

Compilation of Research Work:

- Analyze data using statistical software to evaluate method performance.
- Compile the research work using collected data and perform statistical validation.

Research Publication:

- Prepare and submit the research findings for publication in relevant scientific journals.

6. Importance of the Study:

►International status:

Globally, the integration of green chemistry and QbD principles in pharmaceutical analysis is being actively pursued. The International Conference on Harmonization (ICH) guidelines, particularly ICH Q8, Q9, and Q10, provide a framework for implementing QbD in pharmaceutical development. (Singh & Sharma, 2014). Researchers worldwide are focusing on developing environmentally friendly analytical techniques that comply with stringent regulatory standards. Studies have shown that green chemistry can significantly reduce waste, energy consumption, and hazardous by-products in drug synthesis and formulation. Innovative technologies like continuous flow chemistry, microwave-assisted synthesis, and biocatalysts are being explored to streamline production processes while minimizing environmental impact. (Kumar et al., 2023) However, challenges such as technological barriers, economic viability, and scalability issues remain, necessitating collaborative efforts to overcome these obstacles and promote the widespread adoption of green analytical methods.

►National Status:

In India, there's a growing focus on creating eco-friendly analytical methods for pharmaceuticals using green chemistry and Quality by Design (QbD) principles. Recent studies have highlighted the urgent need for sustainable practices in pharmaceutical analysis to reduce environmental impact. Researchers are exploring the use of green solvents like ethanol and water, and advanced techniques such as ultra-high-performance liquid chromatography (UHPLC) to cut down on waste and energy consumption. (Mehta et al., 2024). Efforts are also being made to integrate QbD principles to enhance the efficiency and robustness of these methods. (Chakraborty & Mondal, 2023) However, there's still a significant gap in research specifically targeting the development of green analytical methods, indicating a need for further exploration and innovation in this area.

Need for the Study:

In recent years, the pharmaceutical industry has increasingly prioritized sustainable practices, recognizing the environmental impact of traditional analytical methods. Conventional techniques often involve the use of hazardous chemicals and solvents, which pose significant risks to the environment. This has led to a growing demand for the development of environmentally friendly analytical methods that do not compromise on sensitivity, specificity, or accuracy. (Mehta et al., 2024, Nakov et al., 2023)

The significance of this research lies in its potential to revolutionize pharmaceutical analysis by introducing sustainable practices that address the environmental and health concerns associated with traditional analytical methods.

Environmental Impact of Traditional Methods: In the pharmaceutical industry often use highly hazardous chemicals and solvents. The high analytical techniques employed can cause significant damage to both the environment and human populations.

Need for New Methods in Analysis: There is a pressing need for new analytical methodologies or techniques that do not compromise sensitivity and specificity while reducing the environmental footprint. These new methods would result in a more sustainable approach to pharmaceutical analysis.

Technological Advancement: Technologies such as high-performance liquid chromatography and mass spectrometry have the potential to produce more efficient, cost-effective, and less polluting methods. These advancements can significantly contribute to the development of greener analytical techniques.

Regulatory Compliance: The research aims to develop environmentally friendly analytical techniques that meet the stringent regulatory standards set by bodies such as the FDA and ICH. Compliance with these standards is essential for the adoption and acceptance of greener methods in the industry.

Benefits of Sustainable Techniques: Adopting sustainable analytical techniques can lead to reduced operational costs and lower waste disposal expenses. Additionally, these techniques contribute to public health by reducing harmful emissions into the environment.

Research Goals: The primary goals of this research are to explore novel analytical methods and contribute to scientific innovation in the development of green pharmaceutical analysis. This research aims to address environmental issues associated

with traditional practices, promote sustainability, public health, and regulatory compliance, and open doors for more sustainable practices in the pharmaceutical sector.

7. Proposed Work Plan

Following table shows Year-wise work plan for the proposed research:

Sr. no.	Name of Activity	Tentative duration (in Months)	Tentative duration (in Year)
1.	Literature survey	06	03
2.	Selection API and Formulation	03	
3.	Procurement of API and Chemicals	03	
4.	Selection of Solvent for Analytical methods	03	
5.	Developing of Analytical Methods using QbD	06	
6.	Assessment of Method for its Greener Approach through Software's	03	
7.	Validation of Developed Methods	03	
8.	Compilation, interpretation of data.	03	
9.	Research Publication	03	
10.	Compilation of Research Work & Thesis Writing	03	
	Total	36	

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